

Listing of Claims 1-31

Claim 1 (cancelled)

Claim 2 (withdrawn) A method for restoring the plasma level of anti-thrombin and/or activated protein C and/or tissue factor pathway inhibitor in a mammal by administering a partial inhibitor of factor VIII to the said mammal.

Claim 3 (withdrawn) A method according to claim 1, wherein the partial inhibitor of factor VIII is a ligand, being other than a polyclonal antibody, able to only partially inactivate factor VIII or a complex involving factor VIII when the said ligand is in a physiological excess by binding to a site of factor VIII of the said complex.

Claim 4 (withdrawn) A method according to claim 1, wherein the partial inhibitor of factor VIII is a ligand which is able to inactivate the co-factor activity of factor VII by interfering with a proteolytic cleavage site or the von Willebrand factor or the tenase complex reaction or by inducing a three-dimensional conformational change in factor VIII or by targeting a domain of factor VIII, in particular the C1 domain of factor VIII, or by targeting factor VIII in the factor VIII-von Willebrand factor complex.

Claims 5-12 (cancelled)

Claim 13 (withdrawn) A pharmaceutical composition for the prevention and/or treatment of a disease selected from the group consisting of the systematic inflammatory response syndrome, sepsis, septic, shock, thrombus formation in the microvasculature and disseminated intravascular coagulation in mammals, comprising as an active ingredient a partial inhibitor of factor VIII, being able to only partially inactivate factor VIII or a complex involving factor VIII when the said ligand is in a physiological excess by binding to a site of factor VIII or the said complex, in admixture with a pharmaceutically acceptable carrier.

Claim 14 (withdrawn) A pharmaceutical composition according to claim 13, wherein the partial inhibitor of factor VIII is a ligand other than a polyclonal antibody.

Claim 15 (withdrawn) A pharmaceutical composition according to claim 13, wherein the only partial inactivation by the said active ingredient of factor VIII or of a complex involving factor VIII is at most 99% inactivation.

Claim 16 (withdrawn) A pharmaceutical composition according to claim 13, wherein the only partial inactivation, by the said active ingredient, of factor VIII or of a complex involving factor VIII is at least 25% inactivation.

Claim 17 (withdrawn) A pharmaceutical composition according to claim 13, wherein the partial inhibitor of factor VIII is present in an anti-thrombin and/or activated protein C and/or tissue factor pathway inhibitor plasma level restoring amount.

Claim 18 (withdrawn) A pharmaceutical composition according to claim 13, further comprising a therapeutically effective amount of an anti-thrombotic agent.

Claim 19 (withdrawn) A pharmaceutical composition according to claim 13, further comprising a therapeutically effective amount of heparin.

Claim 20 (withdrawn) A method according to claim 1, further comprising the sequential administration of a therapeutically effective amount of an anti-thrombotic agent.

Claim 21 (cancelled)

Claim 22 (new) A method for preventing and/or treating Systemic Inflammatory Response Syndrome in a mammal by administering a partial inhibitor of factor VIII to the said mammal which is a monoclonal antibody against Factor VIII or an antigen binding fragment of said monoclonal antibody, said antibody or fragment being able to recognize epitopes located in the C1 domain of Factor VIII.

Claim 23 (new) The method according to claim 22, wherein said monoclonal antibody is produced by on purpose immunization in animals.

Claim 24 (new) The method according to claim 22, wherein said monoclonal antibody is produced by on purpose immunization in mouse.

Claim 25 (new) The method according to claim 22, wherein said monoclonal antibody is of class IgG.

Claim 26 (new) The method according to claim 22, wherein said monoclonal antibody is a humanized monoclonal antibody.

Claim 27 (new) The method according to the claim 22, where said monoclonal antibody is the antibody obtainable from the cell line named KRIX 1 deposited with the Belgian Coordinated Collections of Microorganisms under accession number LMBP 5089CB.

Claim 28 (new) The method according to claim 22, wherein said antigen-binding fragment is an Fab, Fab' or F(ab').sub.2, or scFv.

Claim 29 (new) The method according to claim 22, wherein said monoclonal antibody or fragment is administered in an anti-thrombin and/or activated protein C and/or tissue factor pathway inhibitor plasma level restoring amount.

Claim 30 (new) The method according to claim 22, further comprising the sequential administration of a therapeutically effective amount of heparin.

Claim 31 (new) The method according to claim 22, wherein said monoclonal antibody or fragment of said antibody comprises a variable heavy sequence being at least 80% identical to the amino acid sequence depicted in figure 8 and/or a variable light chain sequence being at least 80% identical to the amino acid sequence depicted in figure 9.